Molecular imaging of Parkinson's pathology in p.A53T alpha-synuclein mutation carriers

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Background: α-synuclein is a central player in the pathogenesis of Parkinson's Disease (PD) and a major component of Lewy bodies and neurites. p.A53T α-synuclein gene mutation-associated PD represents the prototypical genetic synucleinopathy. Whether this condition resembles idiopathic PD, involving multiple brain structures in a sequential ascending fashion, as per Braak staging, is unknown. In particular, whether involvement of the serotoninergic system occurs in such subjects, and, if so, its timing relative to the dopaminergic deficit, has not been studied. Furthermore, although astroglial activation and filamentous Tau deposition have been noted in neuropathological studies in such subjects, it is unknown whether these represent early or late events in the disease process. Methods: Advances in positron emission tomography (PET) molecular imaging allow to investigate serotonergic, dopaminergic, tau and astroglia pathology in humans *in vivo*. In this study such PET molecular imaging data from p.A53T α-synuclein mutation carriers will be compared with data from early, established and advanced cohorts of idiopathic PD patients, thus, providing an opportunity to understand the molecular mechanisms underlying premotor stages and the evolution of PD. Results: Three subjects with the p.A53T α-synuclein gene mutation- 2 asymptomatic and 1 symptomatic- have been imaged with the above molecular imaging techniques at King's College, London. Image analysis and recruitment of further subjects are ongoing. Results of these studies will be presented. Conclusion: Ongoing studies using molecular imaging techniques to assess p.A53T α-synuclein gene mutation carriers may provide novel insights into the evolution of the disease, especially in the pre-motor phase.